

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

Claims 1 - 33 (canceled).

34. (withdrawn-currently amended): A process for producing a hyaluronic acid ~~derivative compound~~ which comprises hyaluronic acid bound to an anti-inflammatory drug through a covalent bond via a spacer having a biodegradable region, said process comprising:

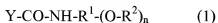
reacting hyaluronic acid with a spacer-bound anti-inflammatory drug, or

reacting a spacer-bound hyaluronic acid with an anti-inflammatory drug,

wherein the anti-inflammatory drug is selected from the group consisting of a non-steroidal anti-inflammatory drug and a disease modifying anti-inflammatory drug.

35. (withdrawn-currently amended): The process for producing a hyaluronic acid ~~derivative compound~~ according to claim 34, which comprises treating a solution of a reaction product of hyaluronic acid with a spacer-bound anti-inflammatory drug or a solution of a reaction product of a spacer-bound hyaluronic acid with an anti-inflammatory drug under alkaline conditions.

36. (new): A hyaluronic acid compound in which a non-steroidal anti-inflammatory drug is bound to hyaluronic acid through a covalent bond, which has a partial structure of a hyaluronic acid disaccharide unit into which the anti-inflammatory drug is introduced, is represented by the following formula (1):



wherein Y-CO- represents one residue of the hyaluronic acid disaccharide unit;

R² represents a non-steroidal anti-inflammatory drug residue represented by Z-CO- or hydrogen atom, with the proviso that all R²'s are not hydrogen atoms;

-HN-R¹-(O-)_n represents a spacer residue in a spacer compound represented by H₂N-R¹-(OH)_n having n numbers of a hydroxyl group;

R¹ represents a linear or branched hydrocarbon group having from 2 to 12 carbon atoms which may have a substituent;

-CO-NH- represents an amide bond of a carboxyl group in glucuronic acid as a constituting saccharide of the hyaluronic acid with an amino group in the spacer compound;

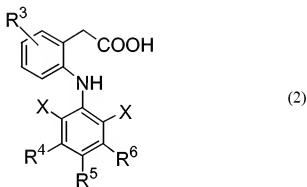
wherein a hydroxyl group in the spacer compound forms an ester bond with a carboxyl group in the non-steroidal anti-inflammatory drug residue; and

n is an integer of from 1 to 3,

wherein the hyaluronic acid compound has a degree of substitution of the non-steroidal anti-inflammatory drug of from 5 to 50 mol% per repeating disaccharide unit of hyaluronic acid, and the carbonyl group in a hyaluronic acid residue constituting the hyaluronic acid compound is present as an amide bond participating in the binding with the spacer-binding anti-inflammatory drug residue or as a free carboxyl group not participating therein, according to the degree of substitution of the non-steroidal anti-inflammatory drug residue.

37. (new): The hyaluronic acid compound according to claim 36, wherein the non-steroidal anti-inflammatory drug is selected from the group consisting of ketoprofen, naproxen, ibuprofen, flurbiprofen, acetylsalicylic acid, felbinac, fenbufen, mefenamic acid, diclofenac and etodolac.

38. (new): The hyaluronic acid compound according to claim 36, wherein the non-steroidal anti-inflammatory drug is a compound represented by the following formula (2):



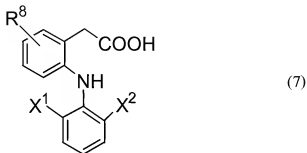
wherein,

R^3 represents a substituent selected from a lower alkyl group and a lower alkoxy group, or a hydrogen atom;

R^4 , R^5 and R^6 each independently represents a substituent selected from a group consisting of a lower alkyl group, a lower alkoxy group and a hydroxyl group, a halogen atom, or a hydrogen atom; and

X's are the same or different and each represents a substituent selected from a lower alkyl group and a trifluoromethyl group, or a halogen atom, and at least one of X's is a halogen atom.

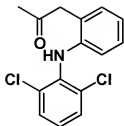
39. (new): The hyaluronic acid compound according to claim 38, wherein the non-steroidal anti-inflammatory drug is a compound represented by the following formula (7):



wherein R^8 represents a substituent selected from a lower alkyl group and a lower alkoxy group, or a hydrogen atom; and

X^1 and X^2 each independently represents a substituent selected from a lower alkyl group and a trifluoromethyl group or a halogen atom, wherein at least one of X^1 and X^2 is a halogen atom.

40. (new): The hyaluronic acid compound according to claim 36, wherein the non-steroidal anti-inflammatory drug residue represented by Z-CO- is a residue represented by the following formula (10):



(10)

41. (new): The hyaluronic acid compound according to claim 36, wherein the hyaluronic acid has a weight average molecular weight of from 500,000 to 3,000,000.

42. (new): The hyaluronic acid compound according to claim 36, wherein R¹ in formula (1) is an ethylene group, a trimethylene group or a propylene group, which may have a substituent(s).

43. (new): The hyaluronic acid compound according to claim 36, which is obtainable by a method comprising reacting hyaluronic acid with a spacer-bound non-steroidal anti-inflammatory drug, or reacting a spacer-bound hyaluronic acid with a non-steroidal anti-inflammatory drug, and adjusting the reaction solution to alkaline conditions.

44. (new): The hyaluronic acid compound according to claim 36, wherein a solution obtained by dissolving the hyaluronic acid compound in an aqueous medium to a concentration of 1.0% by weight is capable of passing through a porous filter having a pore size of 0.45 μm and a diameter of 25 mm, at a ratio of 2 mL per minute or more at a temperature of 24°C under pressure of 5.0 kg/cm².

45. (new): The hyaluronic acid compound according to claim 36, wherein a solution obtained by dissolving the hyaluronic acid compound in an aqueous medium to a concentration of 1.0% by weight is capable of passing through a porous filter having a pore size of 0.22 μm and a diameter of 25 mm, at a ratio of 2 mL per minute or more at a temperature of 24°C under pressure of 5.0 kg/cm².

46. (new): A hyaluronic acid compound solution which is capable of being pushed out from an injector and which comprises the hyaluronic acid compound according to any one of claims 36 to 45 dissolved in an aqueous medium.

47. (new): The hyaluronic acid compound solution according to claim 46, wherein the aqueous medium is an aqueous medium selected from phosphate buffered saline, saline and water for injection.

48. (new): The hyaluronic acid compound solution according to claim 47, which is sterilized through a filter.

49. (new): A pharmaceutical agent which comprises the hyaluronic acid compound according to claim 36 as an active ingredient and a pharmaceutically acceptable carrier.

50. (new): The pharmaceutical agent according to claim 49, which is an arthritis treating agent, an anti-inflammatory medicament or an analgesic.

51. (new): The pharmaceutical agent according to claim 49, which is useful for parenteral administration.

52. (new): The pharmaceutical agent according to claim 51, which is an injection useful for topical administration.

53. (new): The pharmaceutical agent according to claim 51, which is an injection useful for intra-articular administration.

54. (new): A pharmaceutical agent which is capable of being pushed out from an injector and which comprises a solution in which the hyaluronic acid compound according to claim 36, as an active ingredient, is dissolved in an aqueous medium.

55. (new): A kit for injection of a hyaluronic acid compound, which comprises the hyaluronic acid compound solution according to claim 46, which is filled in an injector capable of pushing out the solution.

56. (new): The kit according to claim 55, wherein the filled solution is the pharmaceutical agent according to claim 49.

57. (new): A medical injection kit which is sealed with a plunger for medicament extrusion in such a manner that it can be slid and which comprises a syringe filled with a solution

Application No.: 10/585,417

in which the hyaluronic acid compound according to claim 36 is dissolved in pharmaceutically acceptable phosphate buffered saline, saline or water for injection.